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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,317	06/15/2006	Nils-Olof Johansson	1003301-000275	3220
21839 7590 11/20/2009 BUCHANAN, INGERSOLL & ROONEY PC POST OFFICE BOX 1404 ALEXANDRIA, VA 22313-1404			EXAMINER SCHLIENTZ, LEAH H	
			ART UNIT 1618	PAPER NUMBER
			NOTIFICATION DATE 11/20/2009	DELIVERY MODE ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/583,317	<b>Applicant(s)</b> JOHANSSON, NILS-OLOF	
	<b>Examiner</b> Leah Schlientz	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 July 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 4-10, 13-19, 21 and 22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 4-10, 13-19, 21 and 22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Acknowledgement of Receipt***

Applicant's Response, filed 7/2/2009, in reply to the Office Action mailed 4/2/2009, is acknowledged and has been entered. Claims 10 and 13-19 have been amended. Claims 1-3, 11, 12 and 20 have been cancelled. Claims 4-10, 13-19, 21 and 22 are pending and are examined herein on the merits for patentability.

### ***Response to Arguments***

Any rejection not reiterated herein has been withdrawn as being overcome by amendment.

Applicant's arguments have been fully considered but they are not persuasive, for reasons set forth hereinbelow.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 4-10, 13-19, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pettersson (WO 98/11922) and Thomsen (US 6,015,545), for reasons set forth in the previous Office Action.

Applicant argues on pages 6-7 of the Response that the inventors have surprisingly found that using ratios of Mn to promoter that are higher than those at which coordination compounds are formed leads to a higher concentration in the liver and thus improved imaging capabilities. Applicant asserts that Table 2a and 2b display Liver Mean Mn (nmol/g) for eleven groups of rats that have been treated with different amounts of Mn, alanine and vitamin D<sub>3</sub>. Applicant compares data from Groups 9, 10 and 11, which are had a Mn:alanine range of 2.67:1, with Groups 3-5 and 6-8, which fall below the claimed Mn: promoter range. Applicant argues that "considering each vitamin D<sub>3</sub> level (20, 10 or 5 IU/kg body weight) separately, the results in Table 2a and 2b clearly demonstrate that a molar ratio or Mn:alanine in the range of from 2:1 to 3:1 results in a higher Liver Mean Mn content as compared to a Mn:alanine ratio lower than the claimed range." Applicant asserts that Table 3 displays Liver Mean Mn (nmol/g) for rats that have been treated with different amounts of Mn, alanine and vitamin D<sub>3</sub>. Applicant compares data from Group 5, which is representative of 2:1 Mn:alanine ratio, with Groups 3 and 4, below the claimed Mn:promoter range and Group 6, which is above the claimed range, as well as comparing Group 7 and 8. Applicant argues that results in Table 3 demonstrate that Liver Mean Mn content is highest when a composition in the claimed Mn:alanine range is used, and that it decreases when using a Mn:alanine ratio that is below or above the claimed range.

This is not found to be persuasive. Applicant is respectfully directed to MPEP 716.02(d). Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of

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nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980). See also *In re Peterson*, 315 F.3d 1325, 1329-31, 65 USPQ2d 1379, 1382-85 (Fed. Cir. 2003) (data showing improved alloy strength with the addition of 2% rhenium did not evidence unexpected results for the entire claimed range of about 1-3% rhenium); *In re Grasselli*, 713 F.2d 731, 741, 218 USPQ 769, 777 (Fed. Cir. 1983) (Claims were directed to certain catalysts containing an alkali metal. Evidence presented to rebut an obviousness rejection compared catalysts containing sodium with the prior art. The court held this evidence insufficient to rebut the *prima facie* case because experiments limited to sodium were not commensurate in scope with the claims.). In the instant case, the claims recite any manganese (II) compound a promoter comprising any amino acid. However, the alleged unexpected results are shown only with  $\text{MnCl}_2$  and alanine. Accordingly, the claims are more broad than evidence that is offered to support Applicant's allegation of unexpected results.

Applicant argues on page 8 of the Response that the quantitative differences in Liver Mean Mn content when using a composition in the claimed Mn:promoter range compared when using a composition outside the claimed range may appear small as set forth in the above-mentioned Tables, but that any increase of the Liver Mean Mn content improves the signal intensity during MRI which will in turn enhance the image obtained.

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This is not found to be persuasive. Per MPEP 716.02, any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (differences in sedative and anticholinergic effects between prior art and claimed antidepressants were not unexpected). In *In re Waymouth*, 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974), the court held that unexpected results for a claimed range as compared with the range disclosed in the prior art had been shown by a demonstration of "a marked improvement, over the results achieved under other ratios, as to be classified as a difference in kind, rather than one of degree." Compare *In re Wagner*, 371 F.2d 877, 884, 152 USPQ 552, 560 (CCPA 1967). In addition, the Examiner respectfully notes that no imaging studies have been provided. To be of probative value, an objective evidence should be supported by actual proof, MPEP 716.01(c). Objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See, for example, *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984) ("It is well settled that unexpected results must be established by factual evidence." "[A]ppellants have not presented any experimental data showing that prior heat-shrinkable articles split. Due to the absence of tests comparing appellant's heat shrinkable articles with those of the

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closest prior art, we conclude that appellant's assertions of unexpected results constitute mere argument."). See also *In re Lindner*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972); *Ex parte George*, 21 USPQ2d 1058 (Bd. Pat. App. & Inter. 1991). The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. In the instant case, Applicant's assertion that any increase in Liver Mean Mn content improves signal intensity during MRI appears to be a mere assertion, since evidence to support improved imaging has not been provided.

Applicant further argues on page 8 of the Response that Petterson relates to the use of manganese and promoters, such as amino acids, for diagnosis of the liver, and that the Mn:promoter ratio described in the reference is from 5:1 to 0.02:1. Applicant argues that the range of Mn to promoter is "particular preferably about 1:5," and that there is nothing in Petterson that would make a person skilled in the art believe that the claimed selected Mn:promoter range of from 2:1 to 3:1 is superior compared to other Mn:promoter ratios.

This is not found to be persuasive. Patents are relevant as prior art for all they contain. See MPEP 2123 (1). "The use of patents as references is not limited to what

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the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989). See also *Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005). In the instant case, one of ordinary skill could have readily prepared contrast agents having the claimed Mn:promoter ratio from the broader ratio provided by Petterson with the expectation of slight variation in liver manganese content. The prior art reference is not limited to the preferred embodiments.

### **Conclusion**

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the



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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-9928. The examiner can normally be reached on Monday-Tuesday and Thursday-Friday 9 AM-5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

LHS